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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/899,575	MEGEDE ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,78-90 and 98-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,78-90 and 98-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/29/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 29 September, 2008. Claims 38 and 78-90 were previously pending in the instant application and new claims 98-103 submitted.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 38, 78-90, and 98-103 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Rochester*, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C. 2004). Claim 38 is directed toward an expression cassette comprising a polynucleotide encoding an immunogenic Env polypeptide having at least 90% identity to the full-length

sequence set forth in SEQ ID NO.: 120. Claims 78-90 are directed toward immunization methods employing said expression cassette. The specification discloses the isolation and preliminary characterization of three novel HIV-1 clade C South African isolates designated 8_5_TV1-C.ZA, 8_2_TV1_C.ZA, and 12-5_1_TV2_C.ZA. SEQ ID NO.: 120 encodes a codon-optimized gp140 envelope glycoprotein with a modified signal sequence and a deletion of the V2 region obtained from isolate 8_2_TV1_C.ZA. This modified Env is approximately 630 amino acids in length. Appropriately drafted claim language directed toward SEQ ID NO.: 120 would be acceptable (i.e., An expression cassette comprising a polynucleotide sequence encoding a codon-optimized modified HIV-1 Env glycoprotein comprising SEQ ID NO.: 120). However, the skilled artisan would reasonably conclude that applicants were not in possession of the broad genus of compounds directed toward any sequence displaying up to 10% genetic unrelatedness to the parent sequence.

The crux of the statutory requirement governing written description is whether one skilled in the art, familiar with the practice of the art at the time of the filing date, could reasonably have found the later claimed invention in the specification as filed. *In re Kaslow*, 707 F.2d 1366, 1375, 217 U.S.P.Q. 1089, 1096 (Fed. Cir. 1983). *In re Wilder*, 736 F.2d 1516, 1520 222 U.S.P.Q. 349, 372 (Fed. Cir. 1984, *cert. denied*, 469 U.S. 1209 (1985). *Texas Instruments, Inc.* v. *International Trade Comm'n*, 871 F.2d 1054, 1063, 10 U.S.P.Q.2d 1257, 1263 (Fed. Cir. 1989). Moreover, the courts have stated that the evaluation of written description is highly fact-specific, and that broadly articulated rules are inappropriate. *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A.

1976). *In re Driscoll*, 562 F.2d 1245, 1250, 195 U.S.P.Q. 434, 438 (C.C.P.A. 1977). It is also important to remember that the true issue in question is not whether the specification enables one of ordinary skill in the art to make the later claimed invention, but whether or not the disclosure is sufficiently clear that those skilled in the art will conclude that the applicant made the invention having the specific claim limitations. *Martin* v. *Mayer*, 823 F2d 500, 505, 3 U.S.P.Q.2d 1333, 1337 (Fed. Cir. 1987).

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor has **possession** of the claimed invention. See, e.g., *Vas-Cath*, *Inc*. v. *Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood* v. *American Airlines*, *Inc*., 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. A

lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. *Fujikawa* v. *Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1996).

The skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention for the following reasons: First, the claims encompass an inordinate number of nucleotide and polypeptide variants. SEQ ID NO.: 120 is 1,986 nucleotides in length and gp140mod.TV1.delV2 is approximately 630 amino acids in length. The claims encompass any sequence that is at least 90% genetically related to the parent sequence. This level of genetic variation at the nucleotide sequence level would encompass approximately $(3^{199})(1986!)/(199!)(1786!)$ or ~1 x 10^{835} variants. Ten percent genetic variation at the amino acid sequence level would result in ~1 x 10^{171} variant polypeptide sequences.[1] Thus, the number of variant polynucleotide and amino acid sequences encompassed by the claim language is clearly beyond the scope of reasonable experimentation. Second, considering the enormous claim breadth, it would require more than a single nucleotide sequence encoding a modified Env to provide adequate support. However, the disclosure does not describe the isolation and characterization of a single variant obtained from SEQ ID NO.: 20. There is no indication from review of the disclosure that applicants

[1] These calculations were performed as follows: $TV=(N^Y)(X!)/(Y!)((X-Y-1)!)$, wherein, TV=the total number of variant sequences, N=the number of amino acids or nucleotides that can be substituted (i.e., if any of the 20 naturally occurring amino acids can be substituted, N=19; if any of the four naturally occurring nucleotides can be substituted, N=3), Y=the number of amino acids/nucleotides in the parent sequence that can be substituted (i.e., if the amino acid sequence is 100 aa in length and 10% genetic variation is allowed, Y=10 [100@10%]), and X=the total sequence length of the sequence of interest.

isolated and characterized and variant sequences. Thus, nothing in the disclosure leads the skilled artisan to any particular nucleotide or amino acid sequence. Once again, there is no evidence in the disclosure to suggest that applicants ever isolated or characterized any epitopic variants. Third, it has been well-documented that single or multiple amino acids substitutions, additions, or deletions can abrogate humoral, T-helper, and cytotoxic T-lymphocyte epitope recognition (Johnson *et al*., 1992; Dai *et al*., 1992; Watkins *et al*., 1993; Fenoglio *et al*., 2000; McLain *et al*., 2001; Liu *et al*., 2006). Thus, the art is highly unpredictable and the skilled artisan cannot predict *a priori* the effects of any given substitution on the immunologic properties of the Env polypeptide. Finally, the case law suggests that applicants must provide more than one or two examples to put them in possession of a large genus. See *In re Gosteli*, 10 U.S.P.Q.2d 1614 (Fed. Cir. 1989) and *Ex parte Kubin*, 83 U.S.P.Q.2d 1410 (Bd. Pat. App. & Int. 2007). Therefore, when all the aforementioned factors are considered *in toto*, the skilled artisan would reasonably conclude that applicants were not in possession of the full genus of variants.

Response to Arguments

Applicants traverse and submit the claim amendments are consistent with Example 11 of the Written Description Guidelines. First, applicants are reminded that each application must be evaluated individually on the merits. The written description materials are guidelines and may not be applicable to each and every application reviewed. Second, the sequence involved in the instant application is considerably larger than

that provided in the training materials. SEQ ID NO.: 120 is 1,986 nucleotides in length and gp140mod.TV1.delV2 is approximately 630 amino acids in length. The claims encompass any sequence that is at least 90% genetically related to the parent sequence. This level of genetic variation at the nucleotide sequence level would encompass approximately $(3^{199})(1986!)/(199!)(1786!)$ or ~1 x 10^{835} variants. Ten percent genetic variation at the amino acid sequence level would result in ~1 x 10^{171} variant polypeptide sequences.[2] Thus, the number of variant polynucleotide and amino acid sequences encompassed by the claim language is clearly beyond the scope of reasonable experimentation. Accordingly, the rejection is proper and hereby maintained.

Scope of Enablement

The previous rejection of claim 38 under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, is hereby withdrawn in response to applicants' arguments and amendments.

Enablement

The previous rejection of claims 78-90 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement

[2] These calculations were performed as follows: $TV=(N^Y)(X!)/(Y!)((X-Y-1)!)$, wherein, TV=the total number of variant sequences, N=the number of amino acids or nucleotides that can be substituted (i.e., if any of the 20 naturally occurring amino acids can be substituted, N=19; if any of the four naturally occurring nucleotides can be substituted, N=3), Y=the number of amino acids/nucleotides in the parent sequence that can be substituted (i.e., if the amino acid sequence is 100 aa in length and 10% genetic variation is allowed, Y=10 [100@10%]), and X=the total sequence length of the sequence of interest.

requirement, is hereby withdrawn in response to applicants' amendment and arguments.

Action Is Final, Necessitated by Amendment

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908 or at Jeffrey.Parkin@uspto.gov.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

04 January, 2009